

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-21 (Cancelled)

Claim 22 (New): A recombinant adenovirus that can replicate and produce infectious viral particles that contains a deletion of a part of the genome of a corresponding unmodified replicating adenovirus between the end of the left ITR (Inverted Terminal Repeat) and the beginning of the sequence encoding E1A (early region 1A), wherein the deleted part does not comprise any of the A_I to A_{XII} encapsidation signals and corresponds to a deletion in the segment between positions 311-319 in SEQ ID NO: 12;

wherein said recombinant adenovirus can replicate and produce infectious viral particles in a host cell permissive to infection by the corresponding unmodified replicating adenovirus not containing said deletion.

Claim 23 (New): The recombinant adenovirus of claim 22, which comprises the E1, E2 and E4 coding regions and the right and left ITRs of the unmodified replicating adenovirus.

Claim 24 (New): The recombinant adenovirus of claim 22, which comprises the E1, E2 and E4 coding regions, the right and left ITRs and the E3 coding region of the unmodified replicating adenovirus.

Claim 25 (New): The recombinant adenovirus of claim 22, wherein the deleted portion comprises all or part of the region of the genome of the original replicating adenovirus corresponding to positions 318 and 401 of SEQ ID NO: 12.

Claim 26 (New): The recombinant adenovirus of claim 22, wherein the deleted portion further comprises:

all or part of the region of the genome of the original replicating adenovirus corresponding to that located between positions 311 and 319 of SEQ ID NO: 12; and/or

all or part of the region of the genome of the original replicating adenovirus corresponding to that located between positions 400 and 439 of SEQ ID NO: 12; and/or

all or part of the region of the genome of the original replicating adenovirus corresponding to that located between positions 438 and 499 of SEQ ID NO: 12.

Claim 27 (New): The recombinant adenovirus of claim 22, which further comprises a heterologous polynucleotide sequence of interest inserted in its genome.

Claim 28 (New): The recombinant adenovirus of claim 27, wherein said heterologous sequence is inserted in the region of the genome corresponding to that located between positions 311 and 319 SEQ ID NO: 12.

Claim 29 (New): The recombinant adenovirus of claim 22, wherein said unmodified replicating adenovirus is a type 2 canine adenovirus.

Claim 30 (New): A recombinant adenovirus of claim 22, wherein said unmodified replicating adenovirus is not a type 2 canine adenovirus.

Claim 31 (New): A pharmaceutical composition comprising the recombinant adenovirus of claim 22.

Claim 32 (New): A method for treating a subject comprising administering the recombinant adenovirus of claim 22 to a subject in need thereof.

Claim 33 (New): The method of claim 32, wherein said subject has cancer.

Claim 34 (New): The method of claim 32, comprising administering an immunogenic composition or vaccine comprising said recombinant adenovirus.

Claim 35 (New): The method of claim 32, wherein said subject is a non-human animal that is a domestic or wild carnivore.

Claim 36 (New): The method of claim 32, wherein said subject is human.

Claim 37 (New): A method for making a recombinant protein comprising introducing the recombinant adenovirus of claim 22 into a host cell for a time and under conditions suitable for expression of a recombinant protein from a nucleic acid of said recombinant adenovirus, and recovering said recombinant protein.

Claim 38 (New): A recombinant pseudoreplicating adenovirus that is able to replicate but is unable to produce infectious particles that contains a deletion of a part of the genome of a corresponding unmodified replicating adenovirus between the end of the left ITR (Inverted Terminal Repeat) and the beginning of the sequence encoding E1A (early region 1A), wherein the deleted part comprises the A_X to A_{XII} encapsidation signals, and does not comprise any of the A_I to A_{IX} encapsidation signals, and which includes a deletion of a

segment corresponding to positions 318-401 in SEQ ID NO: 12, and at most to a segment between positions 311-499 in SEQ ID NO: 12;

wherein said pseudoreplicating recombinant adenovirus is able to replicate but is unable to produce infectious particles in a host cell permissive to infection with the corresponding unmodified adenovirus not containing said deletion.

Claim 39 (New): The pseudoreplicating recombinant adenovirus of claim 38, which comprises the E1, E2 and E4 coding regions, and the right and left ITRs.

Claim 40 (New): The pseudoreplicating recombinant adenovirus of claim 38, which comprises the E1, E2 and E4 coding regions, the right and left ITRs, and the E3 coding region.

Claim 41 (New): The recombinant pseudoreplicating adenovirus of claim 38, which comprises a heterologous polynucleotide sequence of interest inserted in its genome.

Claim 42 (New): The recombinant pseudoreplicating adenovirus of claim 41, wherein said heterologous sequence is inserted in the region of the genome corresponding to that located between positions 311 and 319 of SEQ ID NO: 12.

Claim 43 (New): The recombinant pseudoreplicating adenovirus of claim 38 which is a type 2 canine adenovirus.

Claim 44 (New): A recombinant pseudoreplicating adenovirus of claim 38 which is not a type 2 canine adenovirus.

Claim 45 (New): A pharmaceutical composition comprising the recombinant pseudoreplicating adenovirus of claim 38.

Claim 46 (New): A method for treating a subject comprising administering the recombinant pseudoreplicating adenovirus of claims 38 to a subject in need thereof.

Claim 47 (New): The method of claim 46, wherein said subject has cancer.

Claim 48 (New): The method of claim 46, comprising administering an immunogenic composition or vaccine comprising said recombinant pseudoreplicating adenovirus.

Claim 49 (New): The method of claim 46, wherein said subject is a non-human animal that is a domestic or wild carnivore.

Claim 50 (New): The method of claim 46, wherein said subject is human.

Claim 51 (New): A method for making a recombinant protein comprising introducing the recombinant pseudoreplicating adenovirus of claim 38 into a host cell for a time and under conditions suitable for expression of a recombinant protein from a nucleic acid of said recombinant adenovirus, and recovering a recombinant protein.

Claim 52 (New): A nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule comprising the genome of the recombinant adenovirus of claim 22,

b) a nucleic acid molecule comprising the genome of the recombinant adenovirus of claim 30, and

c) a nucleic acid molecule which consists of a fragment of the molecule a) above and which comprises between 10 and 1,000 bp of the sequence of the original replicating adenovirus located upstream of the deleted portion and between 10 and 5,000 bp of the sequence of the original replicating adenovirus located downstream of the deleted portion.

Claim 53 (New): The nucleic acid of claim 52 which further comprises at least 300 bp of the sequence upstream of the deleted portion in the original replicating adenovirus.

Claim 54 (New): The nucleic acid of claim 52 which further comprises at least 10 and 1,000 bp of the sequence downstream of the deleted portion in the original replicating adenovirus.

Claim 55 (New): A plasmid comprising the nucleic acid molecule of claim 57.

Claim 56 (New): A method for preparing a recombinant adenovirus by means of intermolecular homologous recombination in a prokaryotic cell, comprising:

(a) introducing into a prokaryotic cell: (i) a plasmid comprising the genome of an adenovirus and a first selection gene; and (ii) a previously linearized DNA fragment which comprises a heterologous sequence flanked by sequences which are homologous to those flanking the site of said plasmid where the insertion is to be effected and which includes a second selection gene which differs from the first; and

(b) culturing said prokaryotic cell under selective conditions in order to make it possible to generate and select cells which harbor recombinant plasmids which are expressing the first and second selection genes, and

(c) isolating the genome of said recombinant adenovirus from selected prokaryotic cells.

Claim 57 (New): The method of claim 56, wherein the plasmid employed in step (a) is in circular form.

Claim 58 (New): The method of claim 56, wherein the plasmid employed in step (a) has been previously linearized by being cleaved at a restriction site which is located outside the insertion site.

Claim 59 (New): The method of claim 56, wherein the second selection gene is flanked by two identical or different restriction sites which are absent from the genome of the adenovirus which is included in the plasmid employed in step (a).

Claim 60 (New): The method of claim 56, further comprising (d) transfecting said recombinant genome into a cell line which enables said genome to be amplified and encapsidated in infectious viral particles.